Thrombectomy for Pediatric Stroke
StrokeNet Grand Rounds
7/28/2022

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Speaker Disclosures

I have no financial relationships to disclose.

Non FDA approved treatments and devices are discussed.

What do we need to know about MT in childhood stroke?

Initial management of adult stroke

- Exclude hemorrhage
- *(Confirm AIS)*
- IV tPA, if eligible
- Confirm or exclude a large vessel occlusion
- **Determine candidacy for thrombectomy**
- Medical management to limit expansion/complications

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STROKE

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

Pediatric AIS

- Same goal: Organized approach to brain-directed care to minimize injury
- No evidence-based guidelines

--Relative infrequency of childhood stroke

--Delay to diagnosis

--High incidence of stroke mimics

--Underlying illness/medical complexity

Stroke risk factors

Adults

- Hypertension
- High cholesterol
- Diabetes
- Atrial fibrillation
- Carotid stenosis
- Cigarette use
- Obesity
- Cardiovascular disease
- Obstructive sleep apnea
- Heavy ETOH use
- Older age

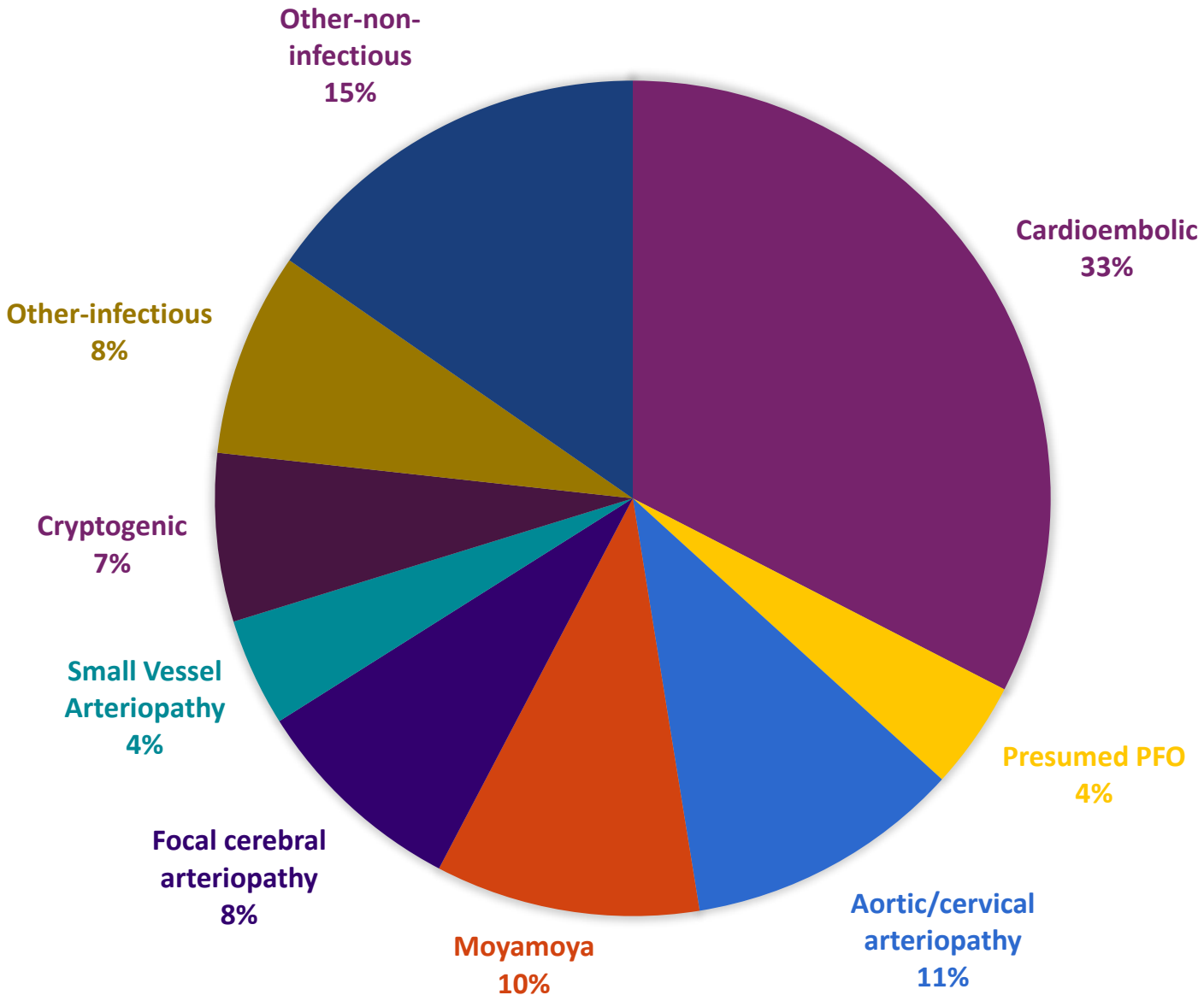
Children

- Cardiac
- Cerebral Arteriopathy
- Sickle Cell Disease
- Chronic systemic illness
- Prothrombotic state
- Acute systemic illness
- Chronic/Acute head and neck disorder
- Infection

(Mackay et al, IPSS, *Ann Neurol*, 2011)

Stroke Etiologies at Seattle Children's Hospital

(unpublished)



Childhood AIS Standardized Classification and Diagnostic Evaluation (CASCADE) (Bernard et al, *Stroke*, 2012)

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Recognizing Acute Neurologic Deficit in childhood

1. Neurologic or non-neurologic? (localization)
2. Stroke or mimic?
   - In adults, sudden focal neurologic deficit is a stroke.
   - In contrast, half of children screened in the hyperacute period have a mimic (Rivkin et al, TIPS, *Stroke*, 2015)

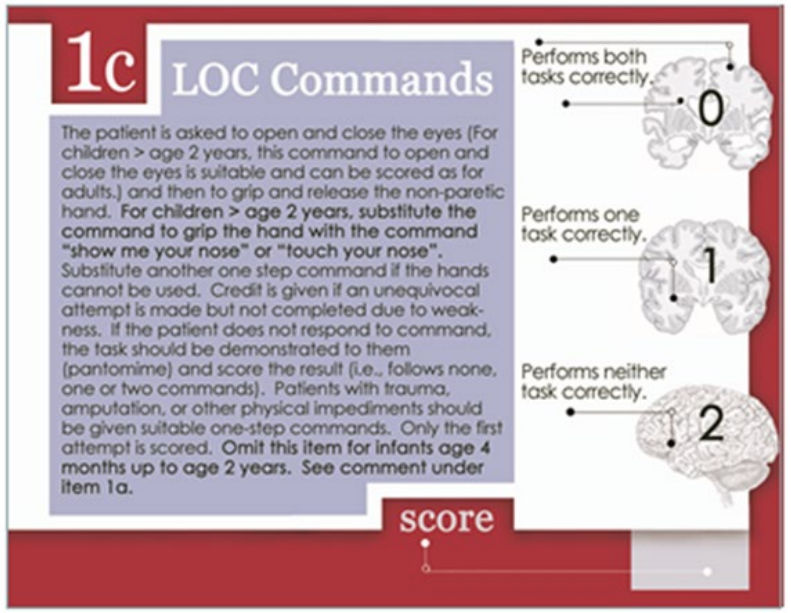
Differential Diagnosis

Urgent mimics
ICH
Mass lesion/Tumor
Infection
PRES
Spinal cord lesion
TIA
Methotrexate toxicity
Urgent non neuro

Assess clinical deficit—Pediatric NIH Stroke Scale

(Ichord et al, 2011)

- Clinical stroke severity—size?
- Deficit consistent with a stroke syndrome?



Consciousness	Facial Movement	Ataxia	Dysarthria
Gaze	Motor Arms	Sensory	Neglect/ Inattention
Visual	Motor Legs	Language	

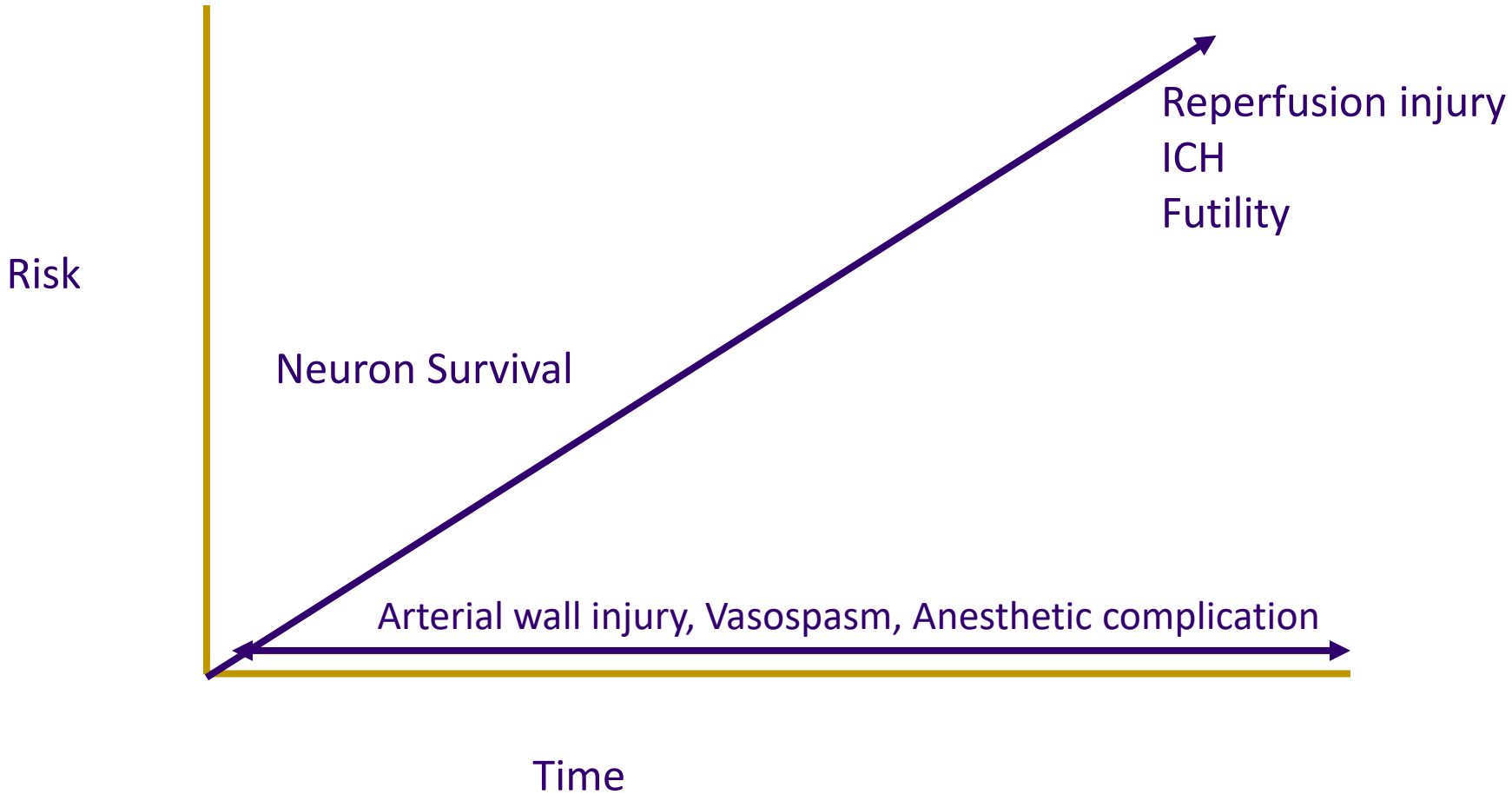
Urgent neuroimaging

4 Questions:
Hemorrhage?
Stroke vs mimic?
Urgent mimic?
Sentinel event?

- Rapid stroke MR protocol
- Sequences:
  - Diffusion weighted imaging (DWI/ADC)
  - T1 weighted
  - T2 weighted (or T2 FLAIR)
  - MR angiography of head and neck
- *Or*, DWI

- Large vessel occlusion?

Recanalization therapy



What about tPA in childhood stroke? (or Tenecteplase or ??)

Benefit of tPA in adults--improved outcome

Time from stroke onset	NNT for benefit	NNT for harm (ICH)
0-90 min	3.6	65
91-180 min	4.3	38
181-270 min	5.9	30
271-360 min	19.3	14

Futility

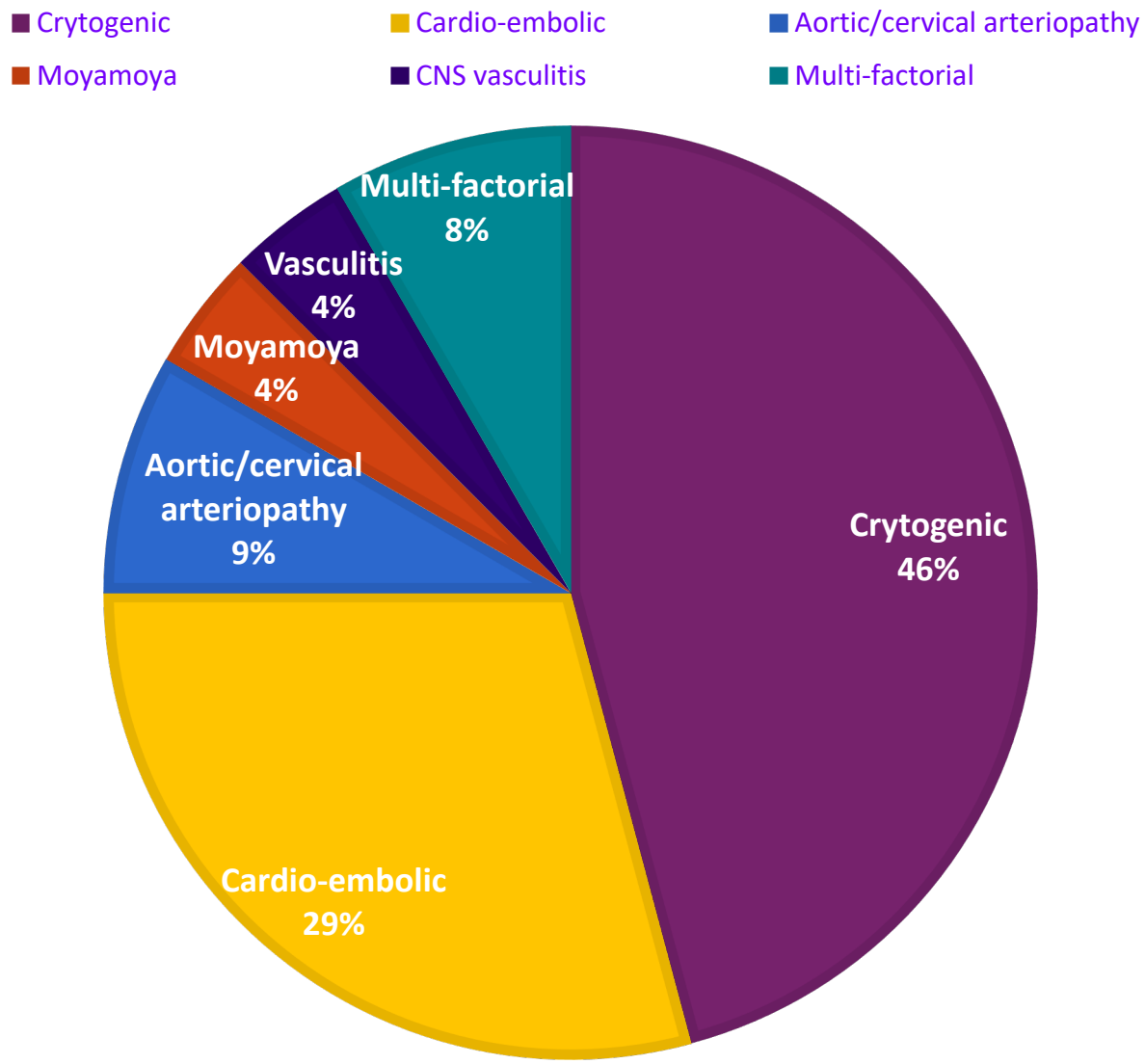
(Pooled data from NINDS 1 and 2, ECASS I and II, and ATLANTIS A and B, from Lansberg et al, *Stroke*, 2009)

TIPSTER (Thrombolysis in Pediatric Stroke Extended Results)

Enroll all children who received IV tPA from former TIPS sites

N = 26

Childhood AIS Standardized Classification and Diagnostic Evaluation (CASCADE) (Bernard et al, *Stroke*, 2012)



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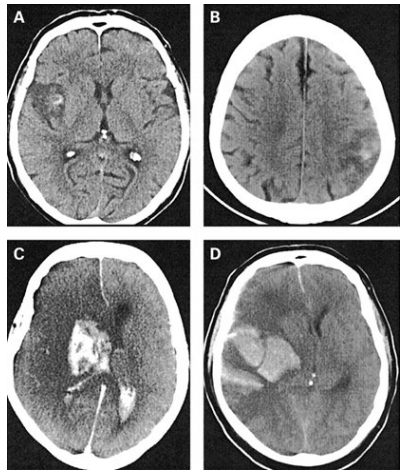
tPA administration and outcome

Patients

- 1.1-17 years (median 14 years)
- Treated within 2-4.5 hours (median 3 hours)
- Dose of IV tPA: 0.9 mg/kg in 24/26
- Circulation:
  - 81% (21): Anterior
  - 19% (5): Posterior



(From Derex L , Nighoghossian N J Neurol Neurosurg Psychiatry 2008)

Post-tPA imaging

- 17 with head CT: No hemorrhage
- 21 with head MRI:

  1 w/scant petechiae (HI1) on GRE, not seen on CT

  1 with confluent petechiae (HI2)

No Symptomatic Intracranial Hemorrhage

No parenchymal hemorrhage 1 or 2

Stroke
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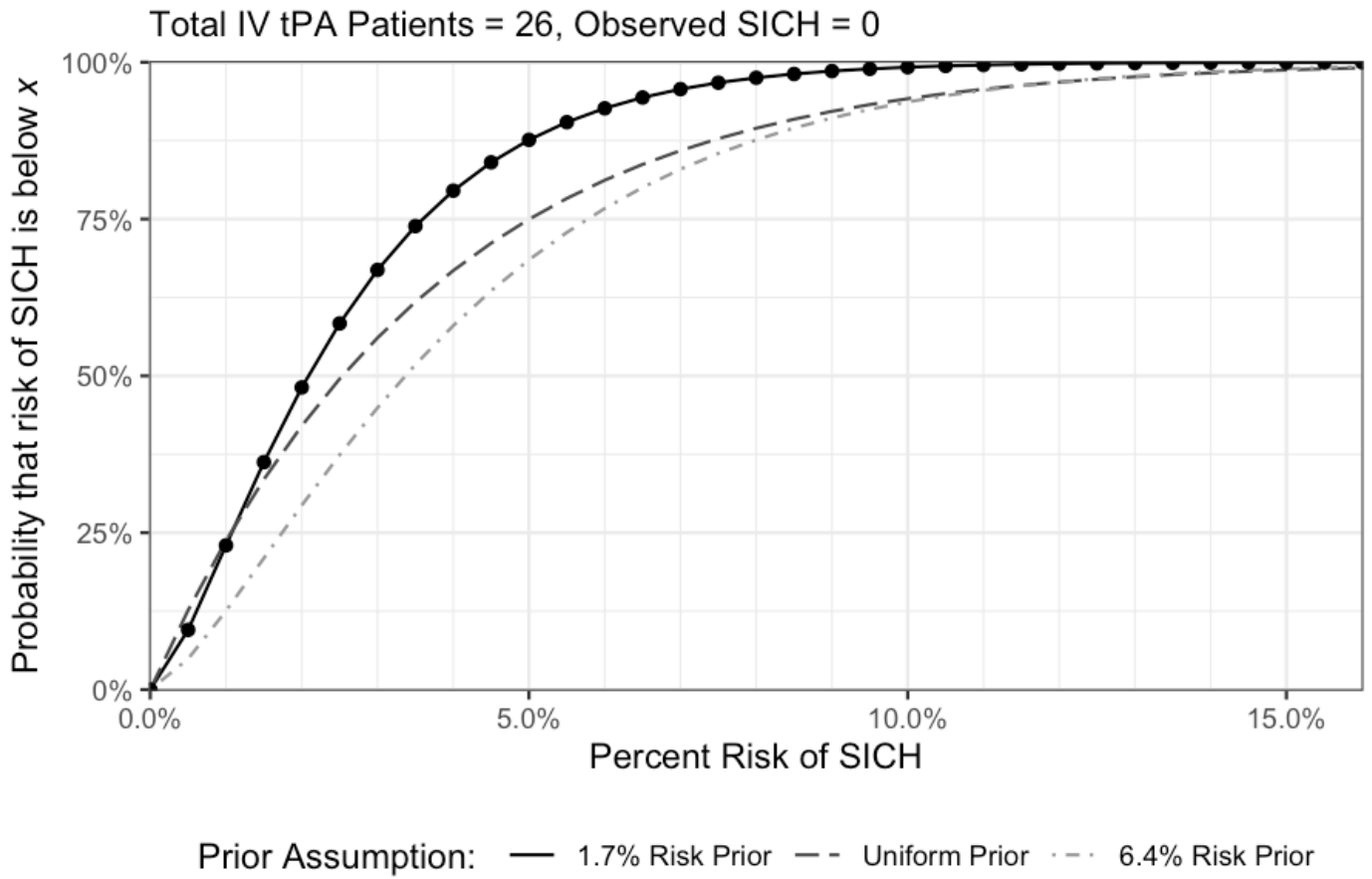
https://doi.org/10.1161/STROKEAHA.119.027225

CLINICAL SCIENCES

Risk of Intracranial Hemorrhage Following Intravenous tPA (Tissue-Type Plasminogen Activator) for Acute Stroke Is Low in Children

Catherine Amlie-Lefond, MD, Dennis W.W. Shaw, MD, Andrew Cooper, PhD, Mark S. Wainwright, MD, PhD, Adam Kirton, MD, MSc, Ryan J. Felling, MD, PhD, Michael G. Abraham, MD, Mark T. Mackay, MBBS, PhD, Michael M. Dowling, MD, PhD, Marcela Torres, MD, Michael J. Rivkin, MD, Eric F. Grabowski, MD, DSci, Sarah Lee, MD, Jonathan E. Kurz, MD, PhD, Hugh J. McMillan, MD, MSc, Dwight Barry, PhD, Jacqueline Lee-Eng, BS, and Rebecca N. Ichord, MD

Estimated risk of SICH: 2.1%



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Is there a Large Vessel Occlusion?

Thrombectomy in selected adult AIS with proximal anterior circulation occlusion

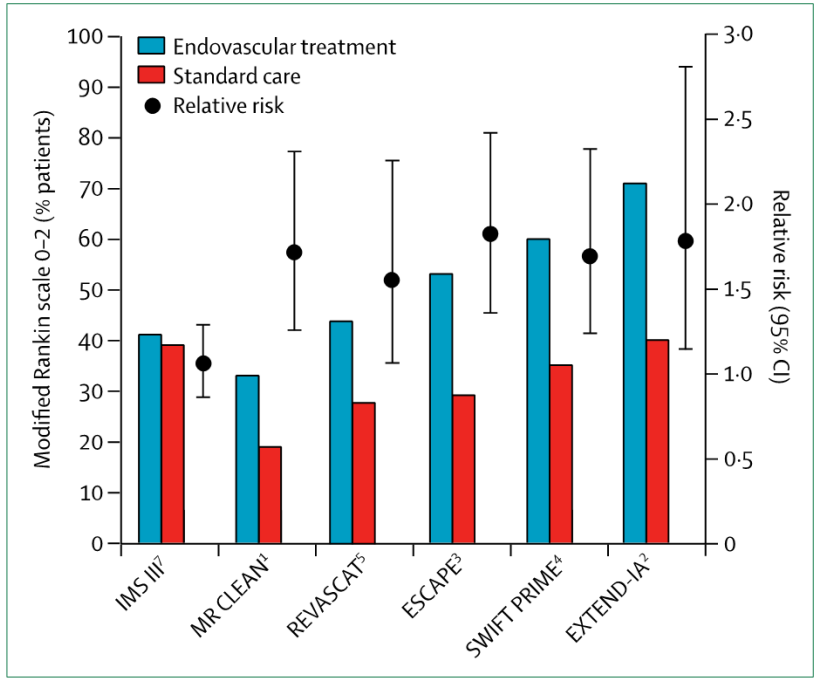
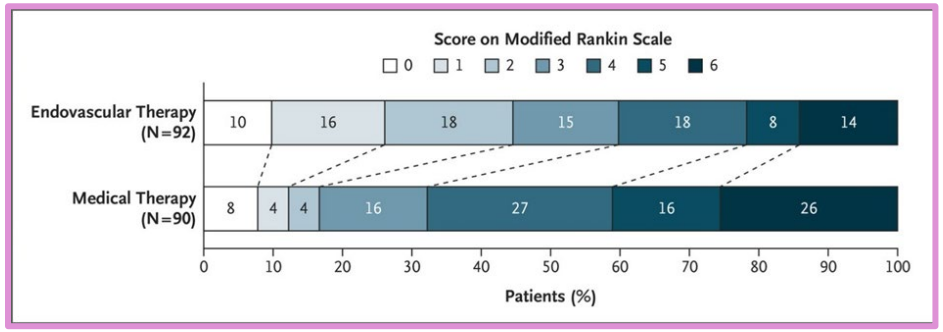


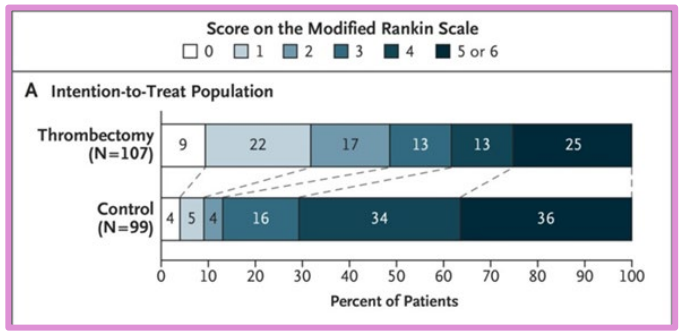
Figure 1: **Functional outcome of patients with ischaemic stroke in trials of endovascular thrombectomy**

Within 6 hours of stroke onset
(From Campbell et al, Endovascular stent thrombectomy: the new standard of care for large vessel ischaemic stroke, *Lancet Neurology*, 2015)

DEFUSE 3: Thrombectomy at 6 to 16 Hours with Selection by Perfusion Imaging
(From Albers et al for the DEFUSE 3 Investigators, *NEJM*, 2018)



DAWN: Thrombectomy at 6 to 24 Hours with a Mismatch between Deficit and Infarct
(From Nogueira et al for the DAWN Trial Investigators, *NEJM*, 2018)



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Published reports of mechanical thrombectomy in childhood AIS

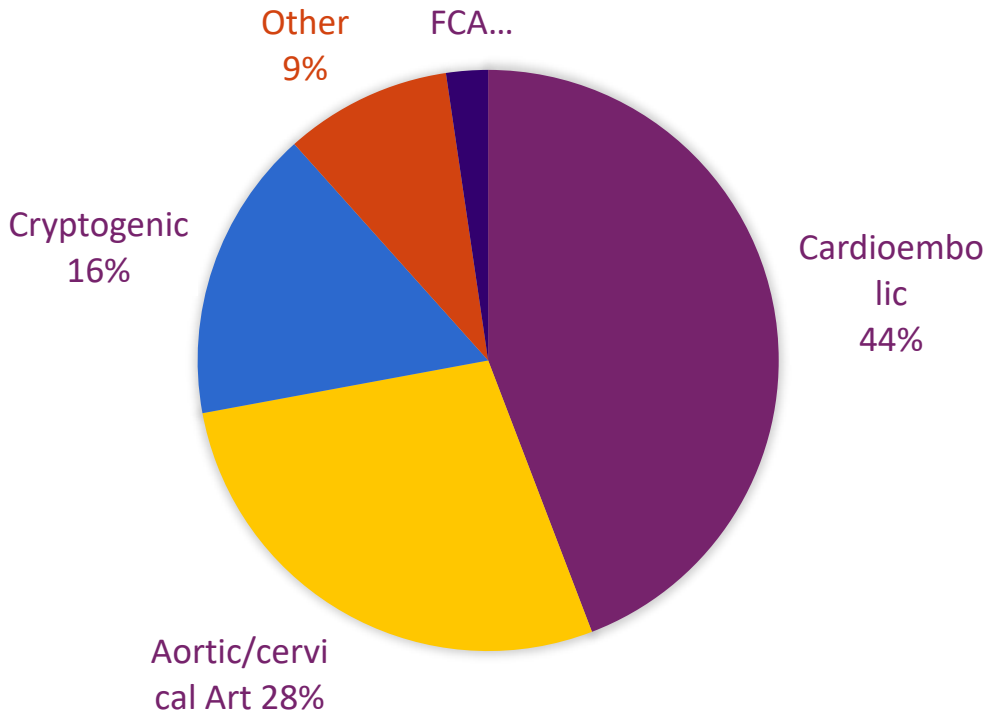
Meta-analyses of published case reports and case series report good short-term outcomes in approximately three-quarters of children.

Case reports and small case series have limited statistical power and publication bias.

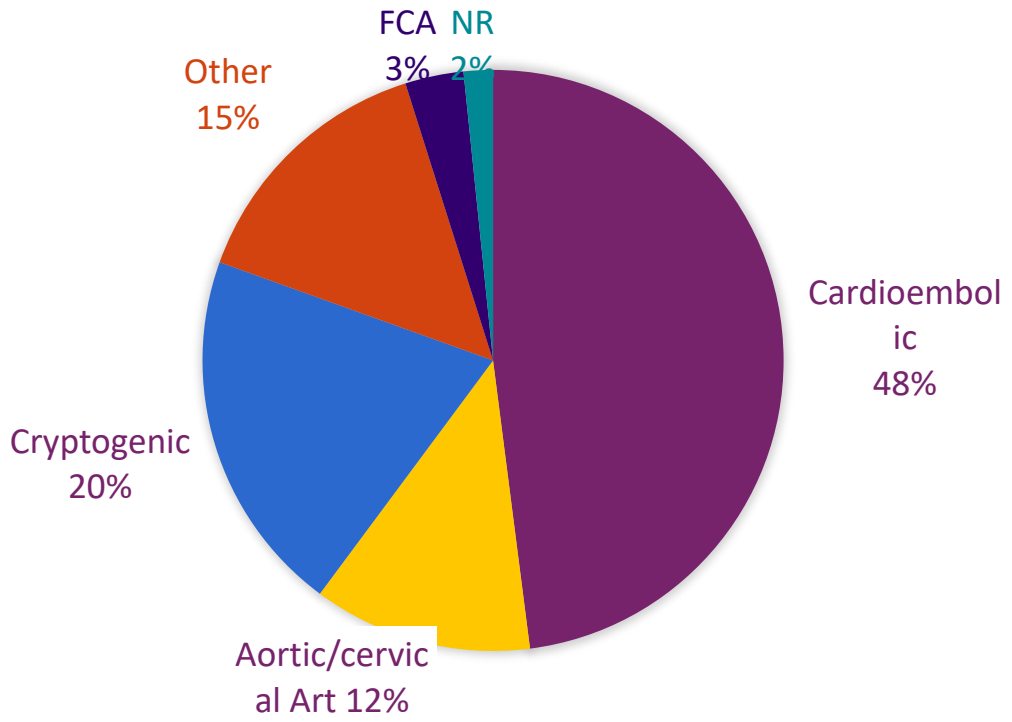
Recanalization in 103 cases with data published prior to 12/31/19	**Outcome**
TICI 3/complete	53% (55)
TICI 2c	4% (4)
TICI 2b	31% (32)
TICI 2a	6% (6)
TICI 1	1% (1)
TICI 0/no recanalization	6% (5)

CASCADE for patients enrolled in TIPSTER compared with published cases

TIPSTER (n=43)
Median age: 12.7 years, median time 5.5 hrs
30% received IV tPA



Literature cases (n=133)
Median age: 11 years (for 103), median time 6 hrs (for 85)
14% received IV tPA



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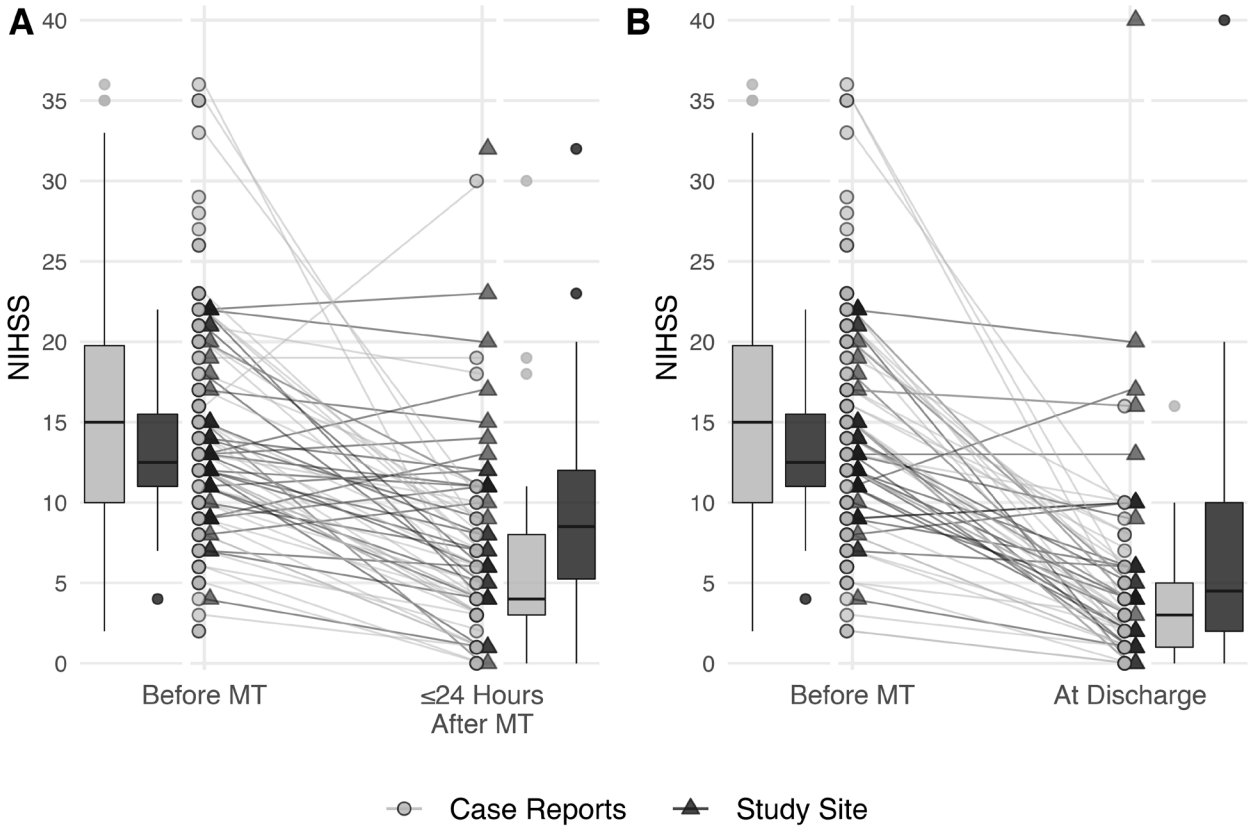
NIHSS before and after MT

	Median NIHSS		
	Before	24 hrs	Discharge
TIPSTER	13	8	4
Literature	15	4	3



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https://doi.org/10.1161/STROKEAHA.120.032009

CLINICAL AND POPULATION SCIENCES

Higher-Quality Data Collection Is Critical to Establish the Safety and Efficacy of Pediatric Mechanical Thrombectomy

See related article, p 1222

Megan Barry, DO, Dwight Barry, PhD, Akash P. Kansagra, MD, MS, Danial Hallam, MD, MSc, Michael Abraham, MD, Catherine Amlie-Lefond, MD, and on behalf of Thrombolysis in Pediatric Stroke (TIPSTER) Investigators*

Study site patients had worse short-term outcomes compared with literature reports & higher rates of NIHSS reporting.

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Pediatric Stroke Outcome Measure (PSOM)

(deVeber et al, JCN, 2020; Kitchen et al, Stroke, 2012; Slim et al, Ped Res, 2020)

5 Subscales

- Right sensorimotor
- Left sensorimotor
- Expressive language
- Comprehension
- Cognition/behavior

Scoring

- 0 = normal
- 0.5 = minimal impairment, normal function
- 1 = mild impairment, slowed function
- 2 = severe impairment, at least 1 missing function

Total PSOM severity classification :

- Normal = 0–0.5 in all subdomains
- Mild = 1 in 1–2 subdomains and < 1 in all remaining subdomains
- Moderate = 1 in ≥ 3 subdomains or 2 in 1 subdomain and < 2 in all remaining subdomains
- Severe = 2 in ≥ 2 subdomains

Can we compare natural history outcomes in Children to Adults?

International Pediatric Stroke Study PSOM at 2 years (Felling et al, 2020)	NINDS mRS in placebo group at 3 months (tPA for Acute Ischemic Stroke-The NINDS rtPA Study, NEJM, 1995)
53.8%: Normal 21.5%: Mild	26%: MRS 0-1
17.2%: Moderate	25%: MRS 2-3
7.5%: Severe	27%: MRS 4-5
	21 %: Death

Which children will benefit?

IV tPA

- Risks vs Benefits
- Developmental hemostasis
- Narrow time window
- New lytics?

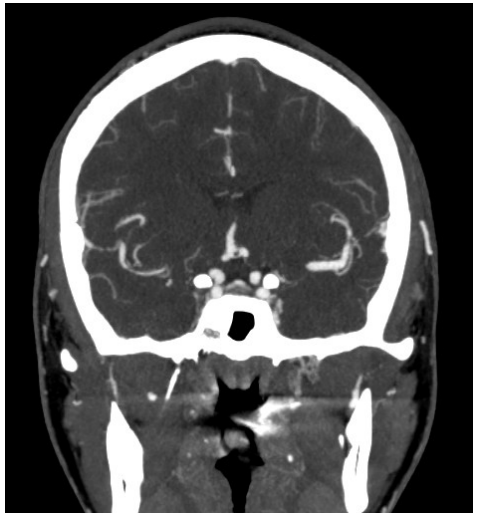
Mechanical thrombectomy

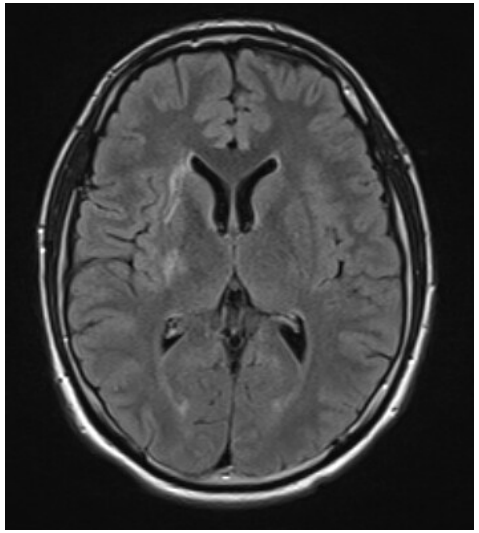
- Risks
- Age (size) cut-off
- Devices
- Penumbral imaging
  - Heart failure
  - Arteriopathy

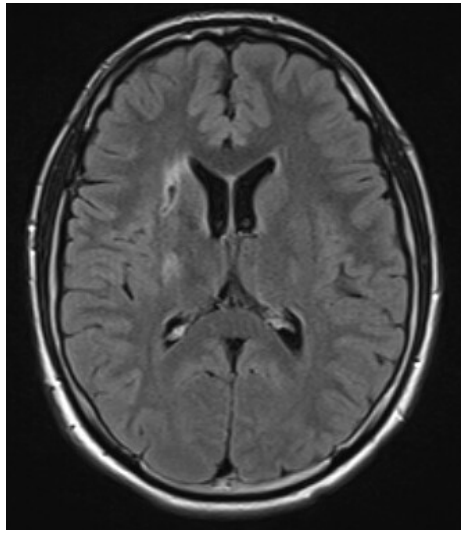
Natural history of childhood AIS?
Biomarkers for benefit and harm?

LVO outcomes can be good in children

Case: Teen with right M1 occlusion







vs

frontiers in Neurology

MINI REVIEW
published: 30 NOvember 2017
doi: 10.3389/fneur.2017.00651

Ischemic Strokes Due to Large-Vessel Occlusions Contribute Disproportionately to Stroke-Related Dependence and Death: A Review

Konark Malhotra[1], Jeffrey Gornbein[2] and Jeffrey L. Saver[3]*

[1] Department of Neurology, West Virginia University, Charleston Division, Charleston, WV, United States, [2] Department of Biomathematics, University of California Los Angeles Comprehensive Stroke Center, Los Angeles, CA, United States, [3] Department of Neurology, University of California Los Angeles Comprehensive Stroke Center, Los Angeles, CA, United States

Background: Since large-vessel occlusion (LVO)-related acute ischemic strokes (AIS) are associated with more severe deficits, we hypothesize that the endovascular thrombectomy (ET) may disproportionately benefit stroke-related dependence and death.

Methods: To delineate LVO-AIS impact, systematic search identified studies measuring dependence or death [modified Rankin Scale (mRS) 3–6] or mortality following ischemic stroke among consecutive patients presenting with both LVO and non-LVO events within 24 h of symptom onset.

Results: Among 197 articles reviewed, 2 met inclusion criteria, collectively enrolling 1,467 patients. Rates of dependence or death (mRS 3–6) within 3–6 months were higher after LVO than non-LVO ischemic stroke, 64 vs. 24%, odds ratio (OR) 4.46 (CI: 3.53–5.63, $p < 0.0001$). Mortality within 3–6 months was higher after LVO than non-LVO ischemic stroke, 26.2 vs. 1.3%, OR 4.09 (CI: 2.5–6.68), $p < 0.0001$. Consequently, while LVO ischemic events accounted for 38.7% (CI: 21.8–55.7%) of all acutely presenting ischemic strokes, they accounted for 61.6% (CI: 41.8–81.3%) of poststroke dependence or death and 95.6% (CI: 89.0–98.8%) of poststroke mortality. Using literature-based projections of LVO cerebral ischemia patients treatable within 8 h of onset, ET can be used in 21.4% of acutely presenting patients with ischemic stroke, and these events account for 34% of poststroke dependence and death and 52.8% of poststroke mortality.

Conclusion: LVOs cause a little more than one-third of acutely presenting AIS, but are responsible for three-fifths of dependency and more than nine-tenths of mortality after AIS. At the population level, ET has a disproportionate benefit in reducing severe stroke outcomes.

Keywords: ischemic, stroke, endovascular, vessel occlusion, morbidity

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JAMA Neurology | Original Investigation

Feasibility, Safety, and Outcome of Endovascular Recanalization in Childhood Stroke
The Save ChildS Study

Peter B. Sporns, MD, MHBA; Ronald Sträter, MD; Jens Minnerup, MD; Heinz Wiendl, MD; Uta Hanning, MD; René Chapot, MD; Hans Henkes, MD; Elina Henkes, MD; Astrid Grams, MD; Franziska Dorn, MD; Omid Nikoubashman, MD; Martin Wiesmann, MD; Georg Bier, MD; Anushe Weber, MD; Gabriel Broocks, MD; Jens Fiehler, MD; Alex Brehm, MD; Marios Psychogios, MD; Daniel Kaiser, MD; Umut Yilmaz, MD; Andrea Morotti, MD; Wolfgang Marik, MD; Richard Nolz, MD; Ulf Jensen-Kondering, MD; Bernd Schmitz, MD; Stefan Schob, MD; Oliver Beuing, MD; Friedrich Götz, MD; Johannes Trenkler, MD; Bernd Turowski, MD; Markus Möhlenbruch, MD; Christina Wendl, MD; Peter Schramm, MD; Patricia Musolino, PhD; Sarah Lee, MD; Marc Schlamann, MD; Alexander Radbruch, MD, JD; Nicole Rübsamen, PhD; André Karch, MD; Walter Heindel, MD; Moritz Wildgruber, MD, PhD; André Kemmling, MD, MHBA

2020

DESIGN, SETTING, AND PARTICIPANTS This retrospective, multicenter cohort study, conducted from January 1, 2000, to December 31, 2018, analyzed the databases from 27 stroke centers in Europe and the United States. Included were all pediatric patients (<18 years) with ischemic stroke who underwent endovascular recanalization. Median follow-up time was 16 months.

EXPOSURES Endovascular recanalization.

MAIN OUTCOMES AND MEASURES The decrease of the Pediatric National Institutes of Health Stroke Scale (PedNIHSS) score from admission to day 7 was the primary outcome (score range: 0 [no deficit] to 34 [maximum deficit]). Secondary clinical outcomes included the modified Rankin scale (mRS) (score range: 0 [no deficit] to 6 [death]) at 6 and 24 months and rate of complications.

RESULTS Seventy-three children from 27 participating stroke centers were included. Median age was 11.3 years (interquartile range [IQR], 7.0-15.0); 37 patients (51%) were boys, and 36 patients (49%) were girls. Sixty-three children (86%) received treatment for anterior circulation occlusion and 10 patients (14%) received treatment for posterior circulation occlusion; 16 patients (22%) received concomitant intravenous thrombolysis. Neurologic outcome improved from a median PedNIHSS score of 14.0 (IQR, 9.2-20.0) at admission to 4.0 (IQR, 2.0-7.3) at day 7. Median mRS score was 1.0 (IQR, 0-1.6) at 6 months and 1.0 (IQR, 0-1.0) at 24 months. One patient (1%) developed a postinterventional bleeding complication and 4 patients (5%) developed transient peri-interventional vasospasm. The proportion of symptomatic intracerebral hemorrhage events in the HERMES meta-analysis of trials with adults was 2.79 (95% CI, 0.42-6.66) and in Save ChildS was 1.37 (95% CI, 0.03-7.40).

CONCLUSIONS AND RELEVANCE The results of this study suggest that the safety profile of thrombectomy in childhood stroke does not differ from the safety profile in randomized clinical trials for adults; most of the treated children had favorable neurologic outcomes. This study may support clinicians' practice of off-label thrombectomy in childhood stroke in the absence of high-level evidence.

Organizing for Acute Arterial Ischemic Stroke in Children

Catherine Amlie-Lefond, MD; Mark S. Wainwright MD, PhD

"Although safety and efficacy have not been systematically studied, case reports suggest that some children with LVO will benefit from mechanical thrombectomy." *Stroke*, 2019

from MT. At the time, the review has been written, several cohort studies had already been published which suggest that MT is a safe and potentially effective treatment option in pediatric LVO.[2,3] These preliminary data have been confirmed by the recently published Save ChildS Study, a retrospective multicenter study including data from 27 stroke centers in Europe and the United States.[4] We, therefore, think that MT in pediatric arterial ischemic stroke patients with LVO should be recommended with more confidence. In this study including 73 pediatric patients who

Editorial, Sporns

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JAMA Neurology | Original Investigation

Incidence and Natural History of Pediatric Large Vessel Occlusion Stroke
A Population Study

Kartik D. Bhatia, MBBS, PhD; Romain Briest, MBBS; Robert Goetti, MBBS; Richard Webster, MBBS; Christopher Troedson, MBBS; Russell C. Dale, MBBS, PhD; Prakash Muthusami, MD; Christina Miteff, MBBS; Ferdinand Miteff, MBBS; John Worthington, MBBS; Kylie Tastula, RN; Timothy Ang, MBBS; Ian Andrews, MBBS

2022

Supplemental content

IMPORTANCE The incidence and natural history of large vessel occlusion (LVO) stroke in children is largely unknown. These knowledge gaps limit the uptake of reperfusion therapies and reduce the efficiency of pediatric acute stroke pathways.

OBJECTIVE To determine the incidence and natural history of pediatric LVO stroke.

DESIGN, SETTING, AND PARTICIPANTS This retrospective population-based cohort study was conducted between January 2010 and December 2019, with a mean (SD) follow-up of 37.0 (28.8) months. Admissions from all pediatric hospitals in the state of New South Wales, Australia, with a final diagnosis of arterial ischemic stroke (AIS) in patients 1 month to younger than 17 years were included. A total of 85 of 251 identified cases were excluded based on selection criteria. Data were analyzed from July 2020 to June 2021.

EXPOSURES One-third of patients with LVO received mechanical thrombectomy with or without intravenous thrombolysis while the remainder were treated conservatively.

MAIN OUTCOMES AND MEASURES The primary outcome was the pediatric modified Rankin Scale (ped-mRS) score 3 months after stroke. Ordinal logistic regression was used to compare non-LVO, LVO without thrombectomy, and LVO with thrombectomy groups.

RESULTS Of 161 included patients, 56 (34.8%) were female, and the mean (SD) age was 6.1 (5.4) years. A total of 166 AIS admissions were studied, and clinical follow-up was available for 164 of 166 admissions. LVO was present in 39 admissions (23.5%). The incidence of LVO stroke was 0.24 per 100 000 patients per year (95% CI, 0.13-0.35). Patients with LVO who did not receive thrombectomy (n = 26) had poor neurological outcomes, with 19 (73.1%) experiencing moderate to severe disability or death (ped-mRS score of 3 to 6) at 3 months (6 of 12 patients receiving thrombectomy [50.0%]; 25 of 38 patients with LVO [65.8%]). Patients with LVO without thrombectomy had significantly worse clinical outcomes than patients with non-LVO at 3 months (odds ratio, 3.64; 95% CI, 1.68-7.87; *P* = .001). Most patients with LVO presented within time windows suitable for thrombectomy (27 of 39 [69.2%] within 6 hours; 35 of 39 [89.7%] within 24 hours).

CONCLUSIONS AND RELEVANCE In this population-based cohort study, the natural history of pediatric patients with LVO stroke treated conservatively was poor, with most experiencing lifelong disability or death. Nearly 90% of pediatric patients with LVO presented within time windows suitable for thrombectomy.

Children with LVO without thrombectomy had significantly worse clinical outcomes than patients with non-LVO at 3 months.

Comparing 13 children with LVO treated with MT with 26 children with LVO not treated with MT:

At 3 months following stroke, ped-mRS score of 3-6:
6 of 12 (50%) with MT
19 of 26 (73%) without MT

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Differences between pediatric and adult AIS

Diagnosis	The diagnosis of pediatric AIS is often delayed. Half of children with suspected stroke have a stroke mimic.
Etiology	Children with AIS have a higher incidence of hematological disease (e.g., sickle cell disease, antiphospholipid antibody syndrome), congenital heart disease, stenosing arteriopathies (e.g., moyamoya, focal cerebral arteriopathy), or intimal injury (e.g., dissection).
Imaging	Perfusion imaging identifies late-presenting adults for MT, but its role in pediatric MT selection is unknown. CT perfusion delivers high radiation dose. Adult-derived metrics of normal and abnormal perfusion have not been validated in children.
Collaterals	Poor collateral flow in adults is associated with poor outcome following EVT. Children often have robust collateral flow, particularly in the setting of progressive arteriopathy.
Location	Posterior circulation AIS is more common in children than in adults.
Deterioration	Early neurologic deterioration is known to occur in adults with LVO. The incidence of early neurologic deterioration in children with LVO is unknown.
Vasospasm	Intraprocedural vasospasm occurs in 3-4% of adult MT but rate and significance is unknown in pediatric MT.
Complications	Adult head size at age 5. Unknown incidence of MT complications in children.

Studying efficacy of MT in children

Probably not feasible

Randomized trial such as DEFUSE 3 and DAWN:

- Infrastructure to enable rapid, round-the-clock randomization and tx would be very expensive.
- Inconvenience or delay in MT will incur risk of non-enrollment as efficacy in adults has led to a loss of clinical equipoise, especially in older children.
- Pragmatic and ethical barrier to unbiased trial enrollment and randomization--children expected to benefit from MT will be treated outside of the trial.

Completely **unbiased natural history cohort**

Possibly possible

Natural history cohort

Perfusion imaging to identify who will benefit (most)

- Availability of timely MR perfusion to avoid radiation dose of CT perfusion
- Establish validity of adult-derived perfusion metrics in children

Immediate recanalization rates

Robust outcomes

Older children and young adults

Studying safety of MT in children

Probably not feasible

- **Capturing impact** of blood pressure, anesthesia, need for transfer, site of care, etc, on outcome.
- Inclusion of **highest risk children**.
- Capturing experience with MT in children in **nonacademic centers**.

Possible

- **Who** decides and who does it
- Capture **immediate adverse events** (vessel injury, bleeds, vasospasm, etc)
  - Compare to adult adverse events
- **Registries and Standardized Data Collection**
  - Need for standardized data collection across sites to gain insight into utility of perfusion imaging and other predictors of outcome.
  - Accepting descriptive safety outcomes—outliers are not likely to appear in statistically coherent cohorts.

Clinical data		
Patient characteristics	• Patient age and sex • Co-morbidities • Pre-morbid mRS • Antithrombotic medications	• Co-morbidities (congenital/acquired heart disease, cerebral arteriopathy, thrombophilia, hemoglobinopathy, rheumatologic/inflammatory disorder, connective tissue disorder, malignancy, genetic or metabolic disease)
Hospital characteristics	• Stroke accreditation (Joint Commission) • Hospital type (pediatric vs adult)	• Previous year AIS/EVT volumes • CTA/MRI availability
Pediatric experience	• ED physician • Neurologist	• Neurointerventionalist • Anesthesiologist
Symptom onset	• Date/time of last known well • Date/time of first known abnormal • Witnessed/unwitnessed onset?	• Patient-reported symptoms: facial droop, focal weakness, speech difficulty, seizure, headache, altered consciousness, vision change, imbalance, other
Initial evaluation	• Field assessment (instrument and score) • Date/time of hospital arrival	• Pediatric NIHSS at arrival and pre-EVT
Neuroimaging	• CT/MRI: ASPECTS/pcASPECTS, hemorrhage • CTA/MRA: occlusion location, tandem occlusion, collateral score	• CT/MR perfusion: infarct and mismatch volume • Final infarct size • Date/time of each neuroimaging study
Thrombolysis	• Date/time IV thrombolytics started/completed • Name/dose of IV thrombolytic administered	• Complications of IV thrombolytic administration • If IV thrombolytics not given, why?
EVT	• Date/time of arterial puncture, clot access, successful reperfusion • Occlusion location • Is a tandem occlusion present? • Number of thrombectomy passes & devices used (each pass) • Device malfunction/retention	• Final eTICI score • Intracranial angioplasty and/or stenting? • Extracranial angioplasty and/or stenting? • Additional treatment details (e.g., IA tPA, antiplatelet/anticoagulant) • Post-procedure antiplatelet/anticoagulant agents
Anesthesia	• Anesthesia modality (local, sedation, general)	• Anesthetic agents
Post-EVT care	• Craniotomy/craniectomy needed? • Ventriculostomy/shunt needed? • Delayed endovascular stenting needed?	• Blood transfusion needed? • Vasoactive medications needed? • Access site repair needed?
Adverse events	• Intra-procedural: embolization to new territory, perforation, dissection, vasospasm, device retention or malfunction, retroperitoneal hemorrhage, access site hematoma, access site occlusion • Post-procedural: hemorrhagic transformation, parenchymal hemorrhage, SICH, subarachnoid hemorrhage, intraventricular hemorrhage, malignant edema	• Sepsis • Angioedema • Cardiac arrest • Death
Outcome	• PSOM at 90 days • mRS at 90 days • Pediatric NIHSS at 0-48 hours, discharge or 7 days	• Length of stay • Discharge disposition • Cause of death (if applicable)

How was decision for MT made?

What drove decision?

When?

By whom?

Outcomes beyond MRS

Score	Children
0	No symptoms at all
1	No significant disabilities despite symptoms; behavior appropriate to age and normal further development
2	Slight disability; unable to carry out all previous activities, but same independence as other age- and sex-matched children (no reduction of levels on the gross motor function scale)[28]
3	Moderate disability; requiring some help, but able to walk without assistance; in younger patients adequate motor development despite mild functional impairment (reduction of 1 level on the gross motor function scale)
4	Moderately severe disability; unable to walk without assistance; in younger patients reduction of at least 2 levels on the gross motor function scale
5	Severe disability; bedridden, requiring constant nursing care and attention
6	Dead

Imaging databank-Central imaging review-

Diagnostic neuroimaging:

- ASPECTS/pcASPECTS
- Location of vessel occlusion
- Collateral score
- Intracranial hemorrhage type
- Core infarct volume
- Penumbra volume
- Final infarct volume

Interventional neuroimaging:

- Occlusion location
- Tandem occlusion
- Degree of reperfusion (eTICI)
- EVT complications (vasospasm, dissection, perforation, embolization to new territory)

How to interpret?

Causal Inference:

Statistical calculations can be done using either classical or Bayesian approaches, but the key is in the use of tools like directed acyclic graphs (DAGs).

In a general sense, it's a set of tools that allow one to make causal claims from observational studies (given certain assumptions), which is not possible with traditional stats outside of an RCT.

Door-to-Needle Delays in Minor Stroke

A Causal Inference Approach

Sara K. Rostanski, MD*; Zachary Shahn, PhD*; Mitchell S.V. Elkind, MD, MS; Ava L. Liberman, MD; Randolph S. Marshall, MD, MS; Joshua I. Stillman, MD; Olajide Williams, MD, MS; Joshua Z. Willey, MD, MS

Background and Purpose—Thrombolysis rates among minor stroke (MS) patients are increasing because of increased recognition of disability in this group and guideline changes regarding treatment indications. We examined the association of delays in door-to-needle (DTN) time with stroke severity.

Methods—We performed a retrospective analysis of all stroke patients who received intravenous tissue-type plasminogen activator in our emergency department between July 1, 2011, and February 29, 2016. Baseline characteristics and DTN were compared between MS (National Institutes of Health Stroke Scale score ≤5) and nonminor strokes (National Institutes of Health Stroke Scale score >5). We applied causal inference methodology to estimate the magnitude and mechanisms of the causal effect of stroke severity on DTN.

Results—Of 315 patients, 133 patients (42.2%) had National Institutes of Health Stroke Scale score ≤5. Median DTN was longer in MS than nonminor strokes (58 versus 53 minutes; P=0.01); fewer MS patients had DTN ≤45 minutes (19.5% versus 32.4%; P=0.01). MS patients were less likely to use emergency medical services (EMS; 62.6% versus 89.6%, P<0.01) and to receive EMS prenotification (43.9% versus 72.4%; P<0.01). Causal analyses estimated MS increased average DTN by 6 minutes, partly through mode of arrival. EMS prenotification decreased average DTN by 10 minutes in MS patients.

Conclusions—MS had longer DTN times, an effect partly explained by patterns of EMS prenotification. Interventions to improve EMS recognition of MS may accelerate care. (***Stroke***. 2017;48:1980-1982. DOI: 10.1161/STROKEAHA.117.017386.)

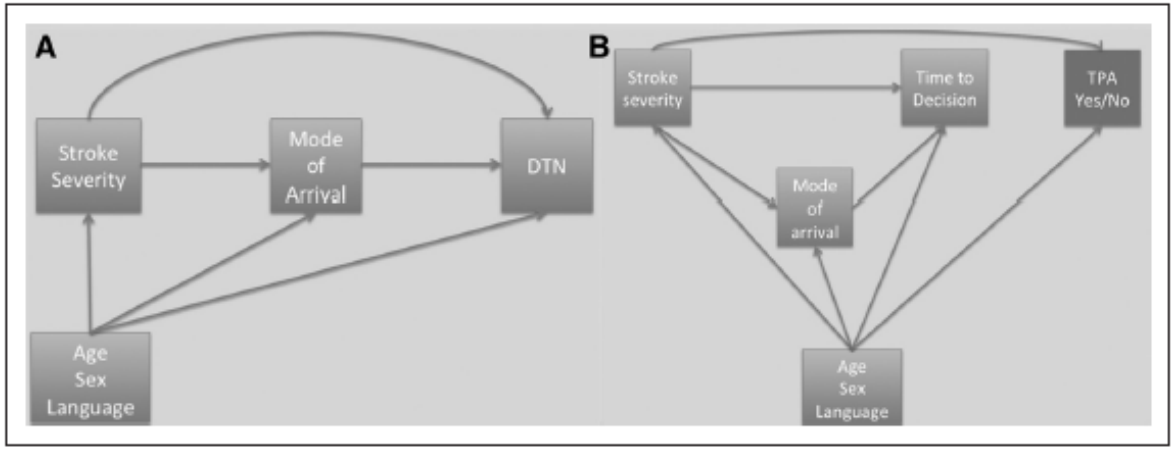


Figure. A, Causal graph representing assumptions necessary to avoid bias from unobserved confounding in all our analyses. Specifically, it communicates the assumptions that there are no common causes of stroke severity and mode of arrival (MOA), stroke severity and door-to-needle (DTN), or MOA and DTN other than age, sex, and primary language. Each individual analysis requires only a subset of these assumptions. **B**, Causal graph that encodes the assumptions necessary to ensure that we did not induce selection bias in any of our causal analyses by restricting the sample only to patients who received IV-tPA (tissue-type plasminogen activator). Specifically, we assume that (1) there are no unobserved common causes of MOA and IV-tPA administration; (2) MOA does not influence whether IV-tPA is administered; and (3) the time until it is determined whether to administer IV-tPA does not influence whether IV-tPA is administered.

Multidisciplinary team

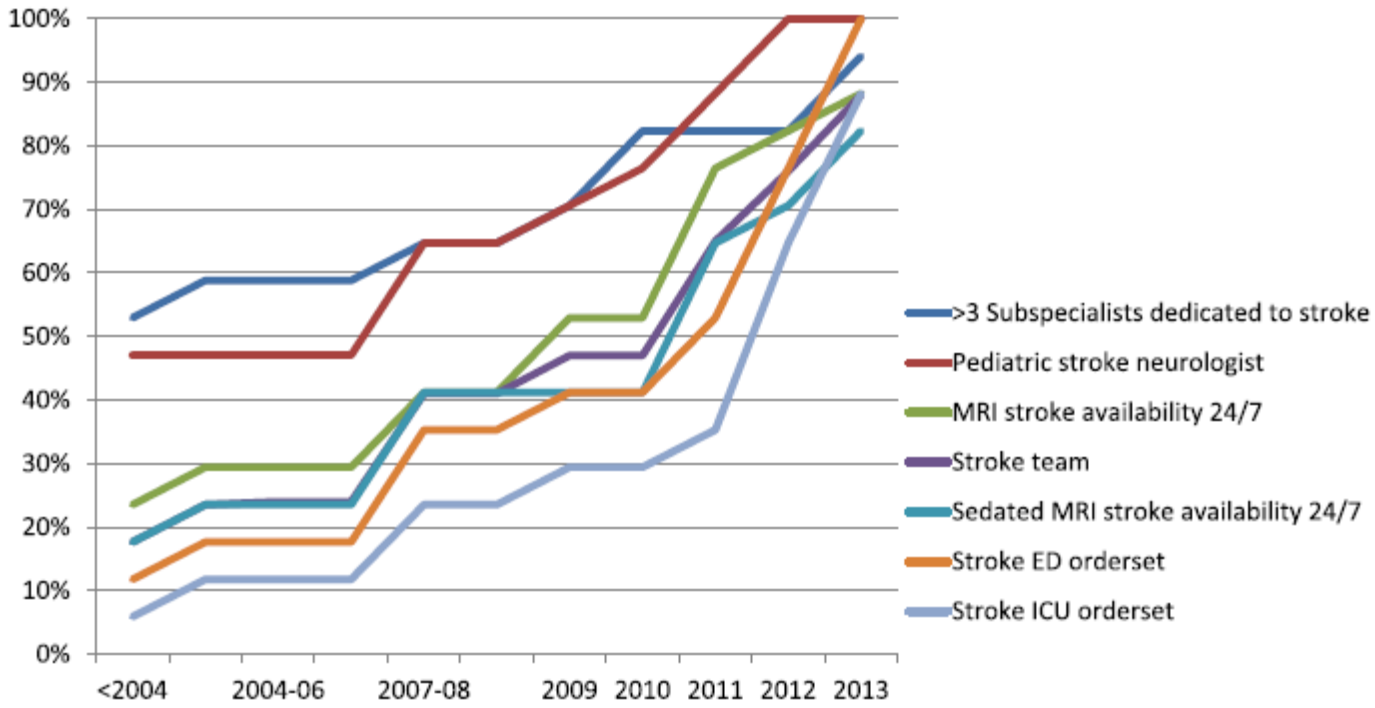
- Pediatric Vascular Neurology
- Pediatric Neurocritical Care
- Neurointervention with pediatric expertise
- Pediatric Neuroradiology
- Pediatric Anesthesia
- Pediatric Emergency and Critical care
- Pediatric Neurosurgery

Stroke
Journal of the American Heart Association

American Heart Association | American Stroke Association

Emergence of the Primary Pediatric Stroke Center: Impact of the Thrombolysis in Pediatric Stroke Trial

Timothy J. Bernard, Michael J. Rivkin, Kelley Scholz, Gabrielle deVeber, Adam Kirton, Joan Cox Gill, Anthony K. Chan, Collin A. Hovinga, Rebecca N. Ichord, James C. Grotta, Lori C. Jordan, Susan Benedict, Neil R. Friedman, Michael M. Dowling, Jorina Elbers, Marcela Torres, Sally Sultan, Dana D. Cummings, Eric F. Grabowski, Hugh J. McMillan, Lauren A. Beslow and Catherine Amlie-Lefond
on behalf of the Thrombolysis in Pediatric Stroke Study



Conclusion

Feasibility
Safety
Imaging
Efficacy
Harm
Benefit

Thank you!

UNIVERSITY of WASHINGTON